REMARKS

A Transmittal Form accompanies this communication. Applicants hereby authorize the Commissioner of the Patent and Trademark Office to charge USPTO Deposit Account No.: 50-0244 for payment of any fees associated with this paper.

In the Office Action mailed 7 December 2004 (hereinafter "Office Action") the Examiner withdrew a number of pending rejections previously set forth in the Final Office Action mailed 7 January 2004. The Examiner has withdrawn the following objection/rejections:

I. The objection to claim 18 made in paragraph 17 of the Office Action mailed 7 January 2004;

II. The rejection of claims 22-32 made in paragraph 13 of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, first paragraph, for allegedly containing new subject matter was withdrawn;

III. The rejection of claim 18 made in paragraph 14(a) of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite was withdrawn;

IV. The rejection of claims 19-29 and 33 made in paragraph 14(c) of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite was withdrawn;

V. The rejection of claim 29 made in paragraph 14(d) of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite was withdrawn;

VI. The rejection of claims 30-32 made in paragraph 14(e) of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite was withdrawn; and

VII. The rejection of claims 18-33 made in paragraph 16 of the Office Action mailed 7 January 2004 under 35 U.S.C. § 1103(a) as allegedly being obvious Granoff (WO 98/58,670) or Ambrosch *et al.* (Bull. WHO 61(2):317-323 [1983]) in view of André *et al.* (In: Modern Vaccinology, (ed.) Kurstak *et al.* Plenum Medical Book Company, New York, NY, *pp.* 41-54, [1994]) and Levine *et al.* (In: Abstracts of the Tenth International Pathogenic *Neisseria* Conference, (Ed) Zollinger *et al.* Baltimore, MD, *pp.* 228-230 [1997]) was withdrawn.

Nevertheless, in the pending Office Action mailed 7 December 2004 the Examiner maintained and/or entered various new rejections. In view of the number and complexity of the pending rejections as well as for the Examiner's convenience, the Applicant provides the respective paragraphs from the instant Office Action which set forth the Examiner's stated rational.

I. Claim 18 stands rejected for the reasons stated in paragraph 14(b) of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite (Office Action, ¶ 14);

II. Claims 19-33 stand rejected for the reasons stated in paragraph 14(f) of the Office Action mailed 7 January 2004 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite (Office Action, ¶ 15);

III. Claims 18-33 stand rejected for the reasons stated in paragraph 15 of the Office Action mailed 7 January 2004 under 35 U.S.C. § 102(b) as allegedly being anticipated by Chong *et al.* (WO 99/42,130) (Office Action, ¶ 16);

IV. Claims 52-55 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly adding new matter (Office Action, ¶ 17);

V. Claims 38-45 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly adding new matter (Office Action, ¶ 18);

VI. Claims 47 and 48 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly adding new matter (Office Action, ¶ 19);

VII. Claims 18-57 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite (Office Action, ¶ 20);

VIII. Claims 34-37, 46, 51, and 54 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chong *et al.* (WO 99/42,130) (Office Action, ¶ 21);

IX. Claims 18-33 and 51 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious under McMaster U.S. 6,146,902 in view André *et al.* (In: Modern Vaccinology, (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, NY, *pp.* 41-54, [1994]), Levine *et al.* (In: Abstracts of the Tenth International Pathogenic *Neisseria* Conference, (Ed) Zollinger *et al.* Baltimore, MD, *pp.* 228-230 [1997]), and Lindberg (Vaccine, 17:S28-S36 [1999]) (Office Action, ¶ 22);

X. Claims 18-36, 46-51, 56, and 57 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, (Vaccine, 10:691-698 [1992]) in view of McMaster, André *et al.*, Levine *et al.*, and Lindberg (Office Action, ¶ 23);

XI. Claim 37 stands rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, Lindberg, and Petre *et al.*, 6,013,264 (Office Action, ¶ 24);

XII. Claims 38-45 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, Lindberg, and Jennings U.S. 5,811,102 (Office Action, ¶ 25); and

XIII. Claims 52-55 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, Lindberg, Avendano *et al.*, (Pediatric Infect, Dis. J., 12:638-643 [1993]) (Office Action, ¶ 26).

The amendments and remarks submitted herein are intended to be fully responsive to the 7 December 2004 Office Action, to advance the prosecution of the present application, and to place the application in condition for allowance. Claims 18-33, 35, 48, 50, and 52 have been amended in order to clarify certain presently claimed embodiments of the invention and to further the Applicant's business interests, but not in acquiescence to the Examiner's arguments. The Applicant reserves the right to prosecute these claims, or similar claims, in the future.

Also claims 37-45, 47, 53, and 55 have been canceled in order to further the Applicant's business interests and to expedite prosecution, but not in acquiescence to the Examiner's arguments. The Applicant reserves the right to prosecute these claims, or similar claims, in the future.

The Applicant has rewritten specification paragraph [0033] in order to better clarify the generic names of the branded compositions recited therein. The amendments to paragraph [0033] do not add new matter and fully supported by the specification as originally filed, and the citation to the reference provide therein.

In the remarks that follow, the Applicant has grouped like rejections together for greater clarity and efficiency. Pending rejections under 35 U.S.C. § 112 are addressed before the Applicant moves onto art based rejections under 35 U.S.C. §§ 102 and 103.

Indefiniteness Rejections Under 35 U.S.C. § 112, Second Paragraph

As an initial matter, the Applicant wishes to thank the Examiner for the many suggestions given for putting the present claims into better form.

I. & II. Claim 18 and Claims 19-33

The Examiner maintains that claim 18, and claims 19-33 dependent thereon, are indefinite for use of the word "derived" in reference to the capsular polysaccharides purified from *N. meningitidis* recited therein. (Office Action, ¶¶ 14 and 15). The specification provides ample description of methods useful for processing capsular polysaccharides from *N. meningitidis* as recited within the context of the presently claimed invention. (*See e.g.*, Specification, ¶¶ 23-26 and 46-55). Nevertheless, in order to advance prosecution the Applicant has removed to term "derived" as suggested.

VII. Claims 18-57

The Examiner has made various indefiniteness rejections over claims 18-57. The rejections at issue are set forth at paragraph 20 of the 7 December 2004 Office Action and in subparagraphs (A) through (V) provided therein. The Applicant addresses the Examiner's concerns in the order in which they were presented. (*See*, Office Action, ¶ 20).

(A) Claim 18

The Applicant must respectfully disagree with the Examiner's comments. Nevertheless, the Applicant has amended claim 18 as suggested by the Examiner to expedite prosecution.

(B) Claims 19-21 and 23-25

The Applicant must respectfully disagree with the Examiner's comments. Nevertheless, the Applicant has amended claims 18, 19, 21, and 23-25 to expedite prosecution.

(C) Claim 52

The Applicant has amended claim 52 to remove the typographical error pointed out by the Examiner.

(D) Claims 18, 26, 29, and 33

The Applicant must respectfully disagree with the Examiner's comments. Nevertheless, the Applicant has amended claims 18, 26, 29, and 33 as suggested by the Examiner to expedite prosecution.

(E) Claims 20 and 21

The Applicant has amended claims 20 and 21 to remove the typographical errors pointed out by the Examiner and to correct antecedence.

(F) Claim 22

The Applicant has amended claim 22 to remove the typographical error pointed out by the Examiner.

(G) & (H) Claims 26 and 27-32

The Applicant must respectfully disagree with the Examiner's comments. Nevertheless, the Applicant has amended claims 26-32 as suggested by the Examiner to expedite prosecution.

(I) (J) & (K) Claim 26, 29 and 33

The Applicant has amended claims 26, 29, and 33 to remove the typographical errors pointed out by the Examiner and to correct antecedence.

(L) (M) & (N) Claim 26, 29, and 33

The Applicant has amended claims 26, 29, and 33 to remove the typographical errors pointed out by the Examiner and to correct antecedence.

(O) & (P) Claim 35

The Applicant has amended claim 35 to provide common chemical and/or structural names for the recited adjuvants and to remove the trade name for the adjuvant described by the chemical formula (N-(2-Deoxy-2-L-leucylamino-β-D-glucopyranosyl)-*N*-octadecyldodecanoylamide hydroacetate).

(Q) Claims 36 and 37

The Applicant has amended claim 35 to remove the typographical errors pointed out by the Examiner and to correct antecedence. As amended, claim 35 provides proper antecedent basis for rejected claims 36 and 37 dependent thereon.

(R) & (S) Claims 38-45

The Applicant has amended claims 38-45 to remove the typographical errors pointed out by the Examiner and to correct antecedence.

(T) Claims 18 and 48-50

The Examiner maintains that claims 18, and 48-50 dependent thereon, are indefinite because for use of the word "derived" in reference to the capsular polysaccharides purified from *N. meningitidis* recited therein. (Office Action, ¶¶ 14, 15, and 20). The specification provides ample description of methods for processing capsular polysaccharides from *N. Mmeningitidis* as recited within the context of the presently claimed invention. (*See e.g.*, Specification, ¶¶ 23-26 and 46-55). As mentioned above concerning rejections I and II, the Applicant amended claim 18 to delete the term "derived" in order to advance the prosecution as suggested by the Examiner. Similarly, the Applicant has amended claims 48-50 to delete the term "derived."

(U) Claim 48

The Applicant has amended claim 48 to remove the typographical error pointed out by the Examiner.

(V) Claims 19-57

The Applicant respectfully submits that the above-mentioned remarks and amendments sufficiently address the Examiner's stated concerns in this rejection.

New Matter Rejections Under 35 U.S.C. § 112, First Paragraph

IV. Claims 52-55

Claims 52 and 54 recite, in pertinent part, a sterile liquid contained in a single-use syringe, and a sterile liquid contained in a vial, respectively. Claims 52 and 54 are dependent upon claim 51, which recites an immunological composition of claim 33 formulated as a sterile liquid. Claim 51 does not stand rejected as allegedly containing new matter. As stated above, claims 53 and 55 have been canceled in order to advance the business interests and the prosecution of the present application and not in acquiescence to the Examiner's arguments. The rejection is thus to moot as to claims 53 and 55.

The Applicant respectfully disagrees with the rejection of claims 52 and 54. (Office Action, ¶ 17). Claims 52 and 54 do not add new matter and are supported by the specification in numerous places. (*See*, Specification, ¶¶ 38-45). For example, the specification states that:

> Compositions of the invention can include liquid preparations . . . and, preparations for parenteral, subcutaneious, intradermal, intramuscular, intraperitoneal or intravenous administration (e.g., injectable administration), such as sterile suspensions or emulsions. Intravenous and parenteral administration are preferred. Such compositions may be in admixture with a suitable carrier, diluent, or excipient such as sterile water, physiological saline, glucose or the like. The compositions can also be lyophilized. The compositions can contain auxiliary substances such as wetting or emulsifying agents, pH buffering agents, gelling or viscosity enhancing additives, preservatives, flavoring agents, colors, and the like, depending upon the route of administration and the preparation desired. Standard texts, such as "REMINGTON'S PHARMACEUTICAL SCIENCE", 17Th edition, 1985, incorporated herein by reference, may be consulted to prepare suitable preparations, without undue experimentation.

(Specification, ¶ 38, emphasis added). The specification thus provides support for sterile liquid preparations administered in various injectable formulations and methods. Furthermore, the specification incorporates the well-respected treatise *Remington's Pharmaceutical Science* 17th (1985)[1] by reference. The Applicant respectfully submits that those skilled in the pharmaceutical, vaccine, and human therapeutics arts readily recognize this treatise as providing

[1] *Remington's Pharmaceutical Science* has since been renamed *Remington: The Science and Practice of Pharmacy*.

detailed information on the formulation, administration and dosing of human therapeutics. Accordingly, the specification and the treatise incorporated therein provide sufficient support for the present claims.

The Examiner appears to be demanding the verbatim recitation "*in haec verba*" in the specification for the present claim terms in claims 52 and 54. The Applicant respectfully submits the Examiner's apparent position is contrary to established patent examining procedure and case law. Notably, the MPEP states that verbatim recitation in the specification of any newly added claim terms is *not required.* Indeed, MPEP § 2163(I)(B) acknowledges that newly added claim terms can be "*supported in the specification through express, implicit, or inherent disclosure.*" (MPEP § 2163(I)(B), emphasis added).

The Applicant must additionally submit that the Examiner's citation of *In re Rasmussen* as support for the instant rejection is not dispositive on the issue. (Office Action, ¶ 17). In *In re Rasmussen*, Chief Judge Markey reversed a decision of the Patent and Trademark Office Board of Appeals affirming the rejection under 35 U.S.C. 132 (112, first paragraph) of a claim at issue as allegedly adding new matter to the specification because it was not based on *in haec verba* support in the specification. (*In re Max Otto Henri Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 [1981]). Chief Judge Markey called the Board's requirement for *in haec verba* support in the specification for every newly added claim term "an exaltation of form over substance." (*See, Rasmussen, p.* 1215, *n.* 7, emphasis added). Chief Judge Markey further stated that "[b]roadening a claim does not add new matter to the disclosure. Disclosure is that which is taught, not that which is claimed." (*Rasmussen, p.* 1214, emphasis added). As noted above, MPEP § 2163(I)(B) acknowledges that the specification can be relied upon as support of all that it expressly, implicitly, or inherently teaches.

The Applicant respectfully requests the withdrawal of the present rejection as he has shown the specification provides sufficient express, implicit, or inherent disclosure for the newly recited claim terms as required by the MPEP and case law.

V. Claims 38-45

Claims 38-45 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. (Office Action, ¶ 18). The Applicant must respectfully disagree.

Nevertheless, in order to advance prosecution and to further his business interests, and not in acquiescence to the Examiner's arguments, the Applicant has canceled claims 38-45.

VI. Claims 47 and 48

Claims 47 and 48 also stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. (Office Action, ¶ 19). The Applicant must respectfully disagree. Nevertheless, in order to advance prosecution and to further his business interests, and not in acquiescence to the Examiner's arguments, the Applicant has canceled claim 47. The rejection is thus moot as to claim 47. Concerning claim 48, the Applicant respectfully submits that the above-mentioned amendment replacing the term "organism" with term "bacterium" sufficiently addresses the Examiner's concerns. Additionally, claim 48 now depends from claim 46. The Applicant thus asks for the withdrawal of the rejection over presently amended claim 48.

Anticipation Rejections Under 35 U.S.C. § 102(b)

III. & VIII. Claims 18-33 and 34-37, 46, 51, and 54

In the aggregate, claims 18-37, 46, 51, and 54 stand rejected as allegedly being anticipated under 35 U.S.C. 102(b) under the reference to Chong *et al.* (WO 99/42,130) (Office Action, ¶¶ 16 and 21). The Applicant must respectfully disagree with the Examiner's arguments. The Applicant will address the Examiner's arguments as they relate to the rejected base claim 18.

As an initial matter, the Applicant wishes to clarify the comments made by Examiner as to the alleged Applicant's position on the Chong *et al.* reference. The Examiner states that:

> Applicant acknowledges that the '130 publication is directed to multivalent immunogenic conjugate molecules comprising a single carrier protein conjugated to multiple, distinct capsular bacterial polysaccharides or tumor antigens, and that the polysaccharides may be selected from different serogroups of a species of bacteria and/or from one or more distinct bacterial species.

Chong *et al.* is directed to multivalent immunogenic compositions consisting of multiple different immunogens (e.g., capsular polysaccharides from different serogroups and/or different

bacteria) each conjugated to an individual T-cell epitope dependent molecule (a carrier protein). The following paragraph from the Summary section of the '130 publication illustrates this point:

> [T]here is provided a multivalent immunogenic molecule compris[ing] a carrier molecule containing at least one functional T-cell epitope, and multiple different carbohydrate fragments each linked to the carrier molecule and each containing at least one functional B-cell epitope.

('130 publication, *p.* 9, *ll.* 12-17, emphasis added). The remaining disclosure of the '130 publication is similarly limited to conjugation of multiple polysaccharides to a single carrier protein. (*See e.g.*, *p.* 9, *ll.* 4-9; *p.* 10, *ll.* 17-22 and *ll.* 30-34; *p.* 11, *ll.* 7-10; *p.* 15, *ll.* 19-21; *p.* 15, *l.* 29 to *p.* 16, *l.* 2; *p.* 20, *ll.* 2-7; *p.* 23, *l.* 22 to *p.* 24, *l.* 10; claims 1, 7, 16, 21, and 23; and, Figures 1 and 9). The preparation of the multivalent immunogenic conjugates is described in Examples 1-10. The analysis of the immunogenicity of the multivalent immunogenic conjugates is described in Examples 11-16. The Applicant maintains that the '130 publication is completely silent as to the instantly claimed subject matter, which as described herein and in previous papers relates to individual immunoconjugates used in combination with one another.

The Applicant would respectfully like to reiterate that the specification of the '130 publication clearly indicates that Figure 9 relates only to the immunogenicity of a meningococcal multivalent immunogenic conjugate. For example, the figure legend on p. 15, lines 19-21 indicates that the figure is demonstrating "rabbit antibody responses to multivalent N. meningitidis oligosaccharides-TT conjugates . . . ." On page 23, lines 28-31, the '130 publication states that Figure 9 shows "that meningococcal [multiple antigenic glycoconjugate] could elicit antibody responses to all three polysaccharides . . . ." Earlier in the same paragraph, it is stated that the conjugates were prepared using "the procedure shown schematically in Figure 1", which illustrates the conjugation of multiple oligosaccharides to a single carrier protein. Thus, Applicants respectfully maintain that Figure 9 does not relate to instantly claimed conjugates, but instead relates only to the multiple immunogenic glycoconjugates described throughout the '130 publication.

The Applicant thus respectfully submits that the '130 publication does not teach every element of the presently claimed invention and that anticipation rejection of claims 18-33 and 34-37, 46, 51, and 54 should be withdrawn. Nevertheless, the Applicant has amended claim 18, and rejected claims 22, 26, 29, and 33 dependent thereon, to further clarify one contemplated and

presently claimed embodiment of the present invention. Presently amended claim 18 recites, in pertinent part, "An immunological composition comprising a combination of two, three, or four distinct and separately made . . . ." The amendments to claims 18, 22, 26, 29, and 33 do not add new matter and are supported by the specification. (*See e.g.*, Specification, ¶¶ 18, 25, 26, 31, and 72).

The Applicant believes that the remarks and amendments presented herein sufficiently address the Examiner's concerns. The withdrawal of the present rejection is respectfully requested.

Obviousness Rejections Under 35 U.S.C. § 103(a)

In summary, all of the pending claims (claims 18-57) stand variously rejected as allegedly being obvious under one or more combinations of references. The Applicant submits that the various obviousness rejections over claims 37-45, 47, 53, and 55 are now moot in view of the Applicant's above-mentioned cancellation of the respective claims.

IX. & X. Claims 18-33 and 51 and 18-36, 46-51, 56, and 57 respectively

For increased clarity and brevity, the Applicant has combined rejections IX (*i.e.*, over claims 18-33 and 51) and X (*i.e.*, over claims 18-36, 46-51, 56, and 57) as they concern rejected independent claim 18 upon which all of the other rejected claims depend.

More particularly, rejection IX sets forth the rejection of claims 18-33 and 51 under 35 U.S.C. § 103(a) as allegedly being obvious under McMaster in view André *et al.*, Levine *et al.*, and Lindberg. (Office Action, ¶ 22). Similarly, rejection X sets forth the rejection of claims 18-36, 46-51, 56, and 57 under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, and Lindberg. (Office Action, ¶ 23). Thus, rejection X encompasses the references cited within rejection IX with the addition of the Costantino *et al.* reference.

Case law and the MPEP require obviousness rejections to be based upon three criteria. Accordingly, a valid *prima facie* case of obviousness exists when the examiner establishes each criterion with sufficient evidentiary support. The three criteria prevent examiners from adopting

impermissible and prejudicial attitudes, such as the use of hindsight, during obviousness examinations. The MPEP § 2143 *et seq.* describes the three criteria as follows:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings [MPEP § 2143.01]. Second, there must be a reasonable expectation of success. [MPEP § 2143.02] Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations [MPEP § 2143.03].

The Applicant respectfully submits that the Examiner has still not established a valid *prima facie* case of obviousness.

The Applicant again respectfully submits that the cited references at best provide a motivation to *try* to develop efficacious combinations of two, three, or four distinct and separately made protein-capsular polysaccharide conjugates as are presently being claimed. Furthermore, it again appears that the Examiner's arguments are based upon an "obvious to try" rationale for modifying and/or combining the cited references. Notably, the Examiner failed to address the Applicant's previous "obvious to try" remarks submitted in the paper mailed 8 September 2004. The Applicant's "obvious to try" remarks are unrebutted.

Likewise, unrebutted are the Applicant's remarks that given the disclosure of Granoff WO 98/58,670 (cited by the Examiner in the Office Action mailed 7 January 2004) one skilled in the art would not expect to successfully make and administer multivalent/tetravalent combinations of protein-capsular polysaccharide conjugates comprising meningococcal serogroups W-135 and Y.

The Federal Circuit has repeatedly held that using an "obvious to try" rational is a legally impermissible basis for attempting to establish a motivation to combine references especially in unpredictable fields such as immunology and vaccinology[2].

[2] "An 'obvious to try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." (*In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 [Fed. Cir. 1990]; emphasis added); "Obvious to [try] is not a proper standard for obviousness. . . . [S]elective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings." (*In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 [Fed. Cir. 1988], emphasis added).

In the Office Action mailed 7 December 2004 the Examiner continues to rely upon Levine *et al.* as supplying a suggestion of successfully "produc[ing] a cost-effective multivalent meningococcal A, C, Y and W-135 polysaccharide-protein conjugate vaccine." (Office Action, ¶¶ 22-26). Levine *et al.*, however, describes a hypothetical cost–effectiveness (C-E) decision model, "using the societal perspective, that compares the costs and benefits from routine infant immunization to the costs and benefits from the current situation where no routine infant immunization exists." (Levine *et al.*, *p.* 228, ¶ 2).

Levine *et al.* focus on the as yet unrealized public health benefits of the hypothetical successful concomitant vaccination of infants with a tetravalent *N. meningitidis* polysaccharide-protein conjugate vaccine and a Hib conjugate vaccine "in the same syringe" as a means of decreasing costs associated with meningococcal disease. As there was no data cited to support Levine's analysis, the authors were forced to make several unsupported assumptions. For example, Levine *et al.* state that:

> [t]he C-E MenConj vaccine in this analysis is based on **some important assumptions**. First, it must be administered in the same syringe with the Hib conjugate vaccine (or other appropriate vaccine), thereby eliminating costs for additional visits or equipment to store and administer the vaccine. Second, we assume that the vaccine will provide 90% protection for at least 4.5 years."

(Levine *et al.*, *p.* 229, ¶ 5, emphasis added). There is no basis however for Levine's assumptions that anti-meningococcal polysaccharide-carrier conjugates would be 90% protective for at least 4.5 years or even that four meningococcal capsular polysaccharide-carrier conjugates would be immunogenic and would not-cross react with the Hib conjugates when administered concomitantly given the unpredictable nature of vaccinology.

The Applicant must also respectfully disagree with the Examiner's continued characterization of the André *et al.* reference as expressly suggesting production of tetravalent meningococcal polysaccharide-carrier conjugate vaccines--no less production of immunogenic compositions comprising a combination of two, three, or four distinct and separately made protein-capsular polysaccharide conjugates as are presently claimed.

André *et al.* states that a number of *non-conjugated* vaccines and immunogenic compositions could potentially be effective against disease caused by *N. meningitidis*. For example, André *et al.*, provide a lengthy discussion of new generations of combination vaccines, including: 1) "vector combined vaccines" (*pp.* 46-48); 2) "microencapsulated combined vaccines" (*pp.* 48-49); 3) "naked DNA combined vaccines" (*p.* 49); 4) "synthetic polypeptide combined vaccines" (*p.* 49-50); and 5) "anti-idiotype vaccines" (*p.* 50). Andre *et al.* describe a number of vaccine technologies without highlighting any one technology as being more promising than another is. The Examiner is respectfully remained that "it is impermissible, within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given proposition, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in art." (*In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 [CCPA 1995]).

In addition to André *et al.*, and Levine *et al.*, the Examiner also refers to references to Costantino *et al.*, McMaster, and Lindberg.

The Applicant previously overcame a rejection based in part on the Costantino *et al.*, reference in his response to the 15 April 2003 Office Action. Costantino *et al.*, do not teach or suggest combinations of two, three, or four distinct and separately made protein-capsular polysaccharide conjugates, wherein each of the conjugates comprises a purified capsular polysaccharide from *N. meningitidis* serogroup of A, C, W-135 or Y conjugated to a carrier protein, wherein at least one serogroup is W-135 or Y as are presently being claimed. The Examiner expressly concedes this point stating "Costantino *et al.* differ from the instant invention in not teaching a vaccine composition comprising a protein-polysaccharide conjugate, wherein the conjugate comprises a purified meningococcal serogroup Y or W-135 capsular polysaccharide conjugated to a carrier protein." (Office Action, ¶ 23).

In the present Office Action, the Examiner restricts use of the Costantino *et al.* to her argument that adjuvanted bivalent (A and C) meningococcal polysaccharide-protein conjugates were known in the art. Thus, the Applicant respectfully submits that the Examiner's arguments are only potentially relevant as to claims 34-36 currently directed to adjuvanted compositions

depending upon base claim 18. As the obviousness/non-obviousness of claims 34-36 is tied to the examination of independent claim 18, the Applicant reserves further comment on Costantino *et al.* until disposition of claim 18.

The Examiner cites the Lindberg reference as providing a reasonable expectation of success. The Examiner argues that Lindberg "expressly taught that so far, all data indicate that meningococcal glycoconjugate vaccines will have [as] great a chance to be successful as the Hib and pneumococcal conjugates." (Office Action, ¶¶ 23, 24, and 26). As there are no detailed tables, graphs, or protocols concerning meningococcal vaccine production or the collection and analysis of data related to meningococcal vaccines on the face of the Lindberg reference as found in relevant section 4.1, likely the "data" to which Dr. Lindberg refers is provided by citations 64-68 referenced therein--although this is not even certain--since the Lindberg fails to definitively specify the quantity or quality of any "data" allegedly considered. The citations are limited to experiences with bivalent (A and C) meningococcal vaccines and do not concern the develop of efficacious combinations of two, three, or four distinct and separately made protein-capsular polysaccharide conjugates as are presently being claimed. Moreover, there is no definitive statement in the Lindberg reference as to exactly what Dr. Lindberg speculates will be potentially licensed in the future. The Applicant respectfully submits that the mere mention of an as then undeveloped and untested multivalent meningococcal vaccine is an insufficient evidentiary basis for combination with the other cited references. Given its many shortcomings, the Lindberg reference fails to provide any guidance or motivation to prepare the presently claimed combinations when taken alone or in combination with the other references.

XI. Claim 37

Claim 37 stands rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, Lindberg, and Petre *et al.*, 6,013,264 (Office Action, ¶ 24). As mentioned above, in view of the Applicant's decision to cancel claim 37 in order to further his business interest, and not in acquiescence to the Examiner's arguments, this rejection is moot. The Applicant reserves the right to prosecute the subject matter of claim 37, or a similar claim, in the future. Likewise, the Applicant also specifically reserves the right to provide remarks concerning the Petre *et al.*, patent in the future.

XII. Claims 38-45

Claims 38-45 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, Lindberg, and Jennings U.S. 5,811,102 (Office Action, ¶ 25). As mentioned above, in view of the Applicant's decision to cancel claim 38-45 in order to further his business interest, and not in acquiescence to the Examiner's arguments, this rejection is moot. The Applicant reserves the right to prosecute the subject matter of claims 38-45, or similar claims, in the future. Likewise, the Applicant also specifically reserves the right to provide remarks concerning the Jennings patent in the future.

XIII. Claims 52-55

Claims 52-55 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious under Costantino *et al.*, in view of McMaster, André *et al.*, Levine *et al.*, Lindberg, Avendano *et al.*, (Pediatric Infect, Dis. J., 12:638-643 [1993]) (Office Action, ¶ 26). The present rejection is based upon the same references as rejections X and XI with the addition of the Avendano *et al.*, reference. As such, the Applicant's remarks concerning rejections X and XI are equally applicable here.

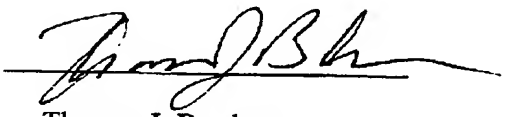
The Examiner's arguments concerning the Avendano *et al.*, reference should fairly be limited to the proposition that the reference teaches the concomitant administration of PRP-T and DTP (group A in the Avendano *et al.*, reference) using a single syringe for deep subcutaneous inoculations. (Office Action, ¶ 26, and Avendano *et al.*, *pp.* 638-639). The reference does not, as the Examiner expressly argues, teach nor suggest the concomitant administration of **any type/number of** capsule polysaccharide-protein glycoconjugate(s) in a single syringe. (Office Action, ¶ 26). Accordingly, the Applicant respectfully submits that the Examiner has grossly overstated the reference. More importantly, however, the reference is silent with respect to the concomitant administration of any one or more of the presently claimed *N. meningitidis* protein-capsular polysaccharide conjugates. The Avendano *et al.*, reference does not add any additional elements to the existing obviousness rejections which have already been more than sufficiently addressed in the proceeding remarks. The Applicant respectfully requests that this rejection be withdrawn.

CONCLUSION

The Applicant respectfully requests entry of this communication and reconsideration of the pending claims in view of the amendments and remarks presented herein. The Applicant believes that the amendments and remarks presented herein are sufficient to overcome all of the Examiner's rejections. Thus, the Applicant respectfully requests the timely mailing of a Notice of Allowance in the instant application. The examiner is encouraged to contact the undersigned if it believed this would expedite prosecution.

Respectfully submitted,

Date: 7 JUNE 2005

By: 

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